

## Abstract

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The invention relates to a device for administration of an aerosol to a mammal, comprising:

- 5       - a chamber provided with gas means, for creating a gas inside the chamber,
- condensation means, for controlling the temperature and or the pressure inside the device, for creating an aerosol from said gas, and
- an opening for releasing the aerosol from the device, wherein
- 10       - the device is provided with control means for manipulating the condensation process in order to thereby control the size of the particles of the aerosol, prior to releasing the aerosol from the opening.

According to the invention the control means are adapted for decreasing the dew point of the aerosol, prior to the release thereof from the opening.

**Device and method for administration of a fluid to a mammal**

The present invention relates to a device for administration of an aerosol to a mammal, comprising a chamber provided with gas means, for creating a gas inside the chamber, condensation means, for controlling the temperature and or the pressure inside the device, for creating an aerosol from said gas, and an opening for releasing the aerosol from the device.

The present invention relates to the field of administration of fluids, such as fluids containing a drug, to the body via the pulmonary route.

Pulmonary drug delivery may be used for respiratory therapy or the immediate uptake and rapid transfer of active substances into the body's systemic circulation through the extensive air-blood interface provided by the lung's capillaries.

With humans, each lung provides more than 100 square meters of surface area. Therefore the lung is a favourable environment for non-invasive delivery and absorption of small and large molecular drugs. Pulmonary drug delivery is already in use for medical gas and a variety of small molecular drugs.

In order to be able to administer drugs it is known to convert pharmaceutical preparations into aerosols, fine powder mists, and vaporous forms for adequate assimilation by the respiratory tract and/or lungs. Inhalation drug therapy is most common in the treatment of pulmonary conditions such as asthma, bronchitis, and emphysema. To ensure desired control over the dosing and deposition rate of active medications into the respiratory tract and/or lungs, inhalation drug therapy usually relies on special delivery devices.

A known device for administration of pharmaceutical preparations according to the introduction is a dry-powder inhaler (DPI). Dry-powder inhalers are breath-actuated devices that use the siphon effect generated by the patient's inhaled air stream to deliver and disperse a drug in fine powder form into the respiratory tract and/or lungs. When using the dry-powder inhaler a person can breath in and thereby inhale a fine powder mist, which is administered to the airways. The mist is generated and administered without the need of strict breathing coordination that is required for the proper use of an MDI (see below). Dry-powder inhalers do not need propellants and preservatives.

A disadvantage of the use of a dry-powder inhaler is the fact that the functional effectiveness of the apparatus depends on the patient's ability to generate adequate respiratory effort and airflow turbulence for disrupting larger powder formations and producing an aerosol of drug particles of respirable size. Thereby, the siphon effect that is used to create the mist does not contribute to the reproducibility of the required dose.

Currently, several design versions of DPI's are available including GlaxoSmithKline's Accuhaler™, Diskhaler™, Rotahaler™, Spinhaler™, and Turbuhaler™.

The Accuhaler™ contains a foil strip of 60 blisters, each containing a unit dose of the drug with a lactose carrier. The Diskhaler™ contains a coarse net that creates turbulence to de-aggregate the drug particles. The drug is contained within four or eight foil-blistered discs, allowing multidose administration. The Rotahaler™ is a single-dose system that uses a coarse net to de-aggregate the drug particles and requires reloading with a capsule containing an appropriate drug dose. The Spinhaler™ is a single-dose system that uses a rotor mechanism to expel the drug and requires reloading with a capsule containing an appropriate drug dose. The capsules required in the Rotahaler™ and the Spinhaler™ may be susceptible to moisture. The Turbuhaler™ releases a unit volume of drug into 2 high-resistance, spiral channels, which create a vortex and optimise particle size when the patient's inspiratory flow rate is greater than 30L/min. This multidose device indicates when 20 doses are left and does not use a propellant, the lack of which reduces coughing and mutes the taste of the drug.

AstraZeneca offers the Pulmicort Turbuhaler™ and the Symbicort Turbuhaler™, a new dry-powder inhaler that offers adjustable dosing, which enables doctors to tailor a patient's treatment with a single inhaler.

Another known device that is used to administer fluids to a mammal via the pulmonary route is a so called metered-dose inhalers (MDI's). This type of device is the most widely used drug-delivery device for inhalation drug therapy of COPD (Chronical Obstructive Pulmonary Disorders). Metered-dose inhalers use propellants from a pressurized container to deposit micronized particles of a drug into the respiratory tract and/or lungs. The propellant is pressurised and mixed with a liquid being or containing a drug. When releasing the mixture from the pressurised container an aerosol is formed with micronized particles of typically 1 – 3 µm.

In the MDI-system the container canister is sealed with a special metering valve designed to release a predetermined volume of drug-containing aerosol in each actuation; however the actual released volume relates to the remaining pressure in the container canister. Within the MDI, the drug is suspended in a propellant with added lubricants and surfactants. Various devices can deliver up to 400 doses; the container's lifetime depends on the volume of drug delivered per actuation.

An advantage of an MDI system, when compared with the above mentioned DPI, is the fact that the systems are resistant to moisture and relatively cheap. An important disadvantage of the MDI-system is the fact that during administration, most particles will travel into the respiratory tract as far as halfway the bronchi. Thereafter the propellant will evaporate, leaving the remaining particles in the bronchi and alveoli, allowing them to travel deeper into the lung system. The fact that the mixture of propellant and active particles is fed into the respiratory tract and the fact that the propellant has to evaporate first in order to allow the particle to move on, creates a time delay when administering the drug to a patient. In addition, exact coordination is required between the actuation of the device and the inhalation. The deposition location of active particles largely depends on the coordination of the created aerosol and the inhalation of a patient. Deposition from an MDI is further affected by the position of the inhaler in relation to the lips, the lung volume at inhalation, the inhaled flow rate and the breath holding of a user after the inhalation (typically for 10 seconds). Other problems include the lack of a dose counter and the "cold Freon" effect, in which the patient stops inhalation as the aerosol reaches the throat. This effect is caused by the low temperature of the mixture entering the body and the reflex of the user not wanting to inhale the cold mixture.

In order to improve the operability of the MDI-systems, a Breath-actuated MDI was developed to improve the efficiency of drug delivery in patients who have difficulty in coordinating their breathing efforts with the working cycle of a conventional pressurised MDI. Breath-actuated MDI's combine conventional MDI's with a spring-driven activation mechanism, which requires priming and is triggered by the patient inhaling at flow rates of 30L/min or more. This requirement limits the usability of the systems, since many patients, such as COPD patients, will not be able to generate the required flow rate.

Breath-actuated MDI's do not require the co-ordination that is necessary with conventional MDI; however, some patients are startled by the release of the spring, which causes glottic closure. This problem may be overcome by using some of the newer MDI's, which feature special, quieter activation mechanisms. The clinical efficacy of a breath-actuated MDI system is equivalent to that of a correctly used conventional MDI system in asthmatics and COPD patients.

A further attempt to improve the use of the MDI's is the use of plastic spacers or holding chambers in order to overcome poor co-ordination of actuation by the patient and the cold Freon effect. Spacers are attached to the exhaust opening and are available in different sizes. Small-volume spacers are available as integral or detachable components of MDI's. Large-volume spacers, which are sold separately and typically replaced every 6 to 12 months, allow the velocity of the aerosol to decrease before inhalation, allowing time for propellant evaporation and reduction in droplet diameter to less than 5µm, thereby improving deposition in the respiratory tract. With large-volume spacers, high-velocity particles are deflected into the inhaled stream, increasing the efficiency of drug delivery. An important drawback of the use of spacers, however, is that repeated actuations of the MDI and delayed inhalation from the spacer is associated with up to 50% loss in drug delivery to the respiratory tract and/or the lungs, as most of the drug is lost in the delivery device or in the patient's mouth and throat due to premature deposition. These effects result from both static electricity and the fact that the half-life of the drug aerosol within the spacer is only 10 seconds. Weekly washing, with the spacer left to stand after rinsing, reduces the level of static electricity.

Due to concerns regarding the impact of chlorofluorocarbon (CFCs) on the earth's ozone layer, the Montreal Protocol – a legally binding international agreement – obliges all parties to reduce, then eliminate, all production and use of ozone-depleting substances, particularly CFCs, which have been used as aerosol propellants. As a result, the new CFC-free DPIs are propelled by the more environmentally friendly hydrofluoroalkanes (HFAs).

To date, only a few CFC-free MDI models (relying on HFA-based propellants) have been launched. However, CFC-free devices are expected to take the place of conventional MDI's in the coming years. For example, Boehringer Ingelheim has recently launched its first HFA-product, the Berotect N<sup>TM</sup>. Other companies offering MDI's include Nektar Therapeutics<sup>TM</sup> and SkyePharma<sup>TM</sup>.



A third type of devices for the administration of fluids according to the introduction is a nebulizer. These devices produce aerosols by either passing compressed air rapidly through a liquid or by vibrating a liquid at a high frequency using ultrasound. Both of these methods provide an effective mist for delivering medications. Pneumatic units are considered superior from the standpoint of depth of delivery, as they produce a finer mist that travels deeper into the lungs, although ultrasonic units are much quieter to operate and do not require a heater.

Despite the fact that the compressor or ultrasound unit represents an equipment investment of at least approximately \$125, the actual nebulizer is nearly always purchased as a disposable to reduce the risk of cross infection. The exception is with patients who are receiving home healthcare; in some of these cases, the patient may prefer to rely on reusable or semi-disposable nebulizers to reduce costs. Treatment nebulizers are small reservoir, handheld updraft devices used for intermittent delivery of medications. They are used primarily in hospitals and for home-based immobilised COPD patients. Medication nebulizers are indicated for the delivery of "custom" doses of bronchodilators, corticosteroids, and mucolytics.

Beside the apparent disadvantage of the price of the device, an important disadvantage of the present nebulizers is the fact that these devices deliver only a fraction of the drug to the deep lung, as most of the drug is lost in the delivery device or in the patient's mouth, throat and upper airways. In addition, the high energy input used for nebulizing will denature macromolecular drugs. The high electrical power requirement also results in a very limited availability of portable instruments. Furthermore, the lungs assimilate a maximum of 25% of the aerosol resulting in high doses of non-assimilated aerosols in the lungs that may disturb the production of naturally produced substances needed to secure proper oxygen assimilation, and may affect the natural resistance mechanism of the lung cells. Other problems include possible (cross) infection due to poor decontamination and difficulties to adjust when converting from using a nebulizer in a hospital to an MDI at home.

AstraZeneca's Pulmicort Respules<sup>TM</sup> is the first nebulized corticosteroid for use with children as young as 12. When the premixed dose of liquid medicine in the respule is opened, the medicine is poured into a nebulizer, which uses a compressor to aerosolise liquid medication, then delivers it via a face mask or mouthpiece. The NIH recognises the nebulizer as an

effective delivery method for infants and young children. Nebulizers are now widely used to deliver nonsteroidal asthma medications. The Pulmicort Respules<sup>TM</sup> is a preventive measure, not a quick-relief treatment, and is not used to treat asthma attacks.

- 5     Inhaled drug delivery is primarily in use to administer single medications; however application-specific drug therapies may require a combination of medicines to be inhaled. Thereto a DPI can be loaded with a capsule containing a mixture of powder drugs; however to deliver a combination of solid and liquid drugs, delivery devices like MDI's or nebulizers must be used because in these types of devices the administered drugs are suspended in a
- 10    liquid. When using existing inhalation drug delivery devices for administering a combination of medicines, the mixture of medications is always made prior to the forming of a powder mist or aerosol. Due to mutual affection, the mixture of medications suffers from degeneration as time passes before inhalation takes place.
- 15    It is further known that the effectiveness of inhaled drug delivery is limited by the poor efficiency of existing pulmonary delivery devices and the difficulty of administering high doses of certain drugs. Existing inhalation drug delivery systems typically deliver only a fraction of the drug to the deep lung, as most of the drug is lost in the delivery device or in the patient's mouth, throat and upper airways. Due to the fact that the patient must co-ordinate the
- 20    breathing manoeuvre with aerosol delivery, dry-powder systems and MDI's also fail to provide the deep-lung dosage reproducibility that is necessary for many systemic applications. In addition, therapeutically valuable macromolecules currently cannot be formulated for use in MDI systems, as macromolecule drugs are denatured by the MDI formulating ingredients. A similar problem is associated with drug nebulization, which also tends to inactivate
- 25    therapeutic macromolecules. Furthermore, dry-powder systems do not provide the protection needed for the long-term stability of macromolecule formulations. Therefore existing inhalation drug delivery systems such as dry-powder inhalers, metered-dose inhalers (MDI's), and nebulizers are used primarily to deliver drugs to the respiratory tract for the treatment of lung diseases.
- 30    With existing inhalation drug delivery devices and currently used methods to create an substance-aerosol, the achieved particle size of the aerosol ranges from 1 to 10  $\mu\text{m}$  and is sometimes even larger; however studies have established that for optimum deposition of peptides and proteins in the deep lung and or the respiratory tract, the aerosol particle size

shall range from 5 nm to 2  $\mu$ m. In addition, the deposition location of aerosol particles in the respiratory tract and lungs is affected by the tidal volume. Existing pulmonary delivery devices do not respond to this problem. Another shortcoming of existing devices is that they are not capable to administer a certain dosage of medication over a predetermined period of time, unless the available dosage in the device is by limited.

#### Summary of the invention

In view of the disadvantages and limitations of the inhalation drug delivery devices according to the prior art, it is an object of the invention to provide a delivery device for administration of a fluid to a mammal via the pulmonary route, by means whereof one or more of the problems related with the use of the known inhalation drug delivery devices can be overcome.

This object is achieved in that the invention provides a device for administration of an aerosol to a mammal, comprising:

- a chamber provided with gas means, for creating a gas inside the chamber,
- condensation means, for controlling the temperature and or the pressure inside the device, for creating an aerosol from said gas, and
- an opening for releasing the aerosol from the device, wherein
- the device is provided with control means for manipulating the condensation process in order to thereby control the size of the particles of the aerosol, prior to releasing the aerosol from the opening.

Because of these features the size of the aerosol particles leaving the device can be carefully determined. The uncontrolled condensation of the aerosol, creating undesired large aerosol particles, can be avoided allowing the aerosol to enter the mammal with a particle size which can be adapted to the use of the aerosol.

In the present text the wording 'mammal' is used. Mammal refers in the text to any human being or animal having a lung system.

In the present invention the wording 'fluid' is used. This refers to any liquid, gas, aerosol or the like.



In the present description the wording 'gas' is used. This refers to a gas that may be created in the device or supplied to the device from outside. It is to be understood that the gas is used as a starting point for creating an aerosol by manipulation of a condensation process, in order to properly control the particle size of the aerosol.

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According to the invention it is possible that the control means are adapted for decreasing the dew point of the aerosol, prior to the release thereof from the opening.

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It is possible that the control means comprise a dilution chamber for mixing the aerosol with a fluid for decreasing the dew point of the aerosol.

This enables the aerosol to be diluted, for instance, by means of an unsaturated gas.

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According to the invention it is possible that the device comprises a gas chamber, provided with the gas means for creating a gas in the gas chamber and a condensation chamber, adjoining the gas chamber, provided with the condensation means for creating an aerosol inside the condensation chamber.

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Thereby it is advantageous that the condensation chamber is provided with temperature means for controlling the temperature of the aerosol inside the condensation chamber.

Moreover, the device provided can be provided with pressure means for controlling the pressure of the aerosol inside the condensation chamber.

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According to the invention it is possible that device comprises a dilution chamber for mixing the aerosol with a fluid for decreasing the dew point of the aerosol, which dilution chamber adjoins the condensation chamber.

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According to a preferred embodiment the gas means comprise a fuel cell.

The fuel cell will use both oxygen and hydrogen in order to produce a gas, heat and power in the form of electricity.

Preferably the opening for releasing the aerosol is adapted to be connected to the mouth of a mammal, in order to generate a flow through the device by means of the respiratory effort of the mammal.

This enables the use of the device as a breath-actuated device.

According to the invention it is possible that the device is provided with a mixer for adding an active substance to the aerosol, prior to or upon release of the aerosol from the opening .

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It is possible that the mixer is provided with a line for supplying the active substance to the mixer in the form of a gas or substance-aerosol. Alternatively, the mixer can be provided with an opening for supplying the active substance to the mixer in the form of a solid or liquid.

10 According to a further aspect of the invention, the invention relates to a method for administration of an aerosol to a mammal, comprising the steps of:

- creating a gas, by means of gas means, inside a chamber,
- condensing of at least part of the gas inside the device, in order to create an aerosol from said gas,

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- releasing the aerosol, and
- administration of the aerosol to the mammal, wherein the method comprises the step of:
- manipulating the condensation process in order to thereby control the size of the particles of the aerosol, prior to releasing the aerosol from the opening.

20 Further features of the method according to the invention are described in the dependent claims.

Below, the invention will be explained in detail with reference being made to the drawings.

The drawings are only intended to illustrate the invention and not to limit its scope which is

25 only defined by the dependent claims.

Fig. 1 shows schematically the productions of a gas by means of a fuel cell;

Fig. 2 shows a fuel cell stack;

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Fig. 3 shows schematically an embodiment of an inhaler with a fuel cell for creating a gas, enclosed in a housing;

Fig. 4 shows the inhaler according to Fig.3 provided with a condenser for creating an aerosol out of said gas;

Fig. 5 shows the inhaler according to Fig. 4 provided with a dilution chamber, for decreasing the dew point of the aerosol;

Fig. 6 shows the inhaler according to Fig. 5 provided with a mixer, for adding an active substance to the aerosol.

Traditional drug delivery methods are used mostly with small molecules, such as individual peptides; however pulmonary drug delivery offers the potential for non-invasive administration of a wide variety of macromolecules. Since the lung provides a large surface area and air-blood interface allowing large-molecule proteins and peptides access to the body's systemic circulation, pulmonary delivery has the potential to be a much more effective route of administration of macromolecules, with a relatively higher bioavailability than with any other alternative delivery route except injection. Nearly every bio-therapeutic product that treats chronic or long-term illness would benefit from non-invasive delivery by providing a competitive advantage with current therapeutics. Pulmonary delivery of macromolecules can extend the life of a drug, increase patient compliance due to prompt effectiveness, and reduce the cost of long-term healthcare. These advantages could expand the market for each product and may enable new therapeutic uses of certain macromolecular drugs. As an alternative to the invasiveness of injection, the development of a deep lung drug delivery system could increase patient acceptance and improve compliance.

It is known that the aerosol particle size largely determines the deposition location in the respiratory tract and the lungs. In 1993, the International Committee for Radiation Protection (ICRP) has adapted a new lung model that indicates the deposition rate in different compartments for particles of a specific size. This universally applied lung model was announced in the ICRP 60 report. The old lung model had the following compartments: Naso-Pharynx (NP), Trachea-Bronchi (TB) and Pulmonary (P). The old deposition model considered the aerodynamic behaviour of particles ranging in size from 0,1 to 10  $\mu\text{m}$  only and predicted >40% deposition in the Pulmonary compartment for particles ranging from 0.1 to 0.5  $\mu\text{m}$ , approx. 10% deposition in the compartment TB over the entire range, and >50% deposition in NP for particles over 2  $\mu\text{m}$ .

In the new lung model – also described by A.S. Keverling Buisman in NVS Publication No. 17, pp.129-134 – the compartments have been renamed and regrouped. Naso-Pharynx (NP) has been renamed to Extra-Thoracic (ET), Trachea-Bronchi (TB) has been split into upper Bronchi up to generation 8 (BB) and lower bronchi from generation 9 to 18 (bb). The latter includes part of the old Pulmonary (P) compartment as far as the respiratory bronchi (generation 16 to 18) are concerned. Finally the remaining part of the Pulmonary (P) compartment is renamed to Alveolar-Interstitial (AI). The latter compartment corresponds with the deep lung. In addition to the aerodynamic behaviour of particles in the range 0,1 to 10  $\mu\text{m}$ , the new deposition model also considers thermodynamic behaviour of aerosols in the range 1 to 100 nm. The new deposition model predicts >50% deposition in ET both for particles >2  $\mu\text{m}$  and < 2nm. Optimum deposition (> 40%) in AI is predicted in the range 5 – 50 nm. Deposition in compartment bb is approx. 35% in the range 1 – 5 nm and <20% for BB for the entire range.

For optimal deep-lung delivery of peptides and proteins, it is important to use the proper aerosol particle size. Studies have established that these particles should range from 5 nm to 50 nm in diameter for optimal deposition efficiency in the deep lung.

In order to be able to administer a substance-aerosol to a mammal via the pulmonary route and thereby achieve a desired deposition effect, the device according to the present invention is equipped with features to manipulate the aerosol particle size during creation and administration of the substance-aerosol.

Configurations of the invention include bench top (clinical), desktop (residential) and palm-size (handheld) delivery devices; however the preferred configuration is a stand-alone personal inhaler (inhalation drug delivery device).

In the preferred configuration of the invention, a personal inhaler, a fuel cell is used to create a gas. The use of the fuel cell is shown in FIG 1.

The fuel cell 1 according to Fig. 1 is an electrochemical device that combines hydrogen 2, from a container 2A, and oxygen 3, from a container 3A, to produce gas 4, heat 5 and



electricity, schematically represented by light bulb 6. Alternatively, the flow of oxygen can be provided by means of the ambient air. This is schematically shown in Fig. 3.

As hydrogen 2 flows into the fuel cell's anode 1A and oxygen 3 into the fuel cell's cathode 1B, the fuel cell produces gas 4 – containing  $H_2O$  molecules – and heat 5. That means that the fuel cell 1 produces a gas with an elevated temperature.

As shown in Fig. 2, individual fuel cells 1, 11, 21, 31 may be combined into a fuel cell "stack" 10 to increase the total electrical power generated.

The process of generating a gas according to Figs. 1 and 2, according to the invention is entrapped in an inhaler. Fig. 3 shows the fuel cell 1 positioned inside an inhaler, schematically represented by cylinder 15. The opening 17 for inhalation is positioned at the right end side of the cylinder 15.

Because of the enclosure 15, the gas generated by the fuel cell 1 will start to condensate in the inhaler and forms an aerosol 16. According to Fig. 3 the required amount of oxygen is provided by the ambient air 18. Alternatively, the oxygen is provided by a container as described with reference to Fig.1.

Upon travelling through the inhaler, from the fuel cell 1 towards the opening 17, the gas molecules generated by the fuel cell 1 continue to condensate causing the aerosol particles to increase in size. This is schematically indicated in Fig. 3 with increasing size of the represented droplets 19. This increase in aerosol particle size is undesired, since the size determines its stability and the deposition effect.

In order to manipulate the aerosol particle size by controlling the condensation process, according to the invention, the inhaler 15 is provided with a temperature controlled condenser 19. This is shown in Fig. 4. The mixture that leaves the condenser 19 is saturated. This temperature controlled condenser 19 is also used to limit the condensation process, thus the mixture leaving the condenser 19 has a predetermined condition. The presence of the condenser 19, limits the space wherein the gas is to be created by means of the fuel cell 1. This enclosed space can be referred to as the gas chamber 14.

In order to stop the condensation process, according to the invention, the aerosol that leaves the condenser 19 is mixed with unsaturated gas, e.g. ambient air, resulting in an unsaturated mixture. Thereto the device is provided with a dilution chamber 20 as shown in Fig. 5. The ratio of unsaturated gas added and the saturated mixture that leaves the condenser, determines the dew point of the unsaturated mixture. The new dew point of the mixture is preferably below the temperature of the mixture leaving the opening 17 and the body temperature. The added gas is preferably of the same temperature as the saturated mixture leaving the condenser 19. By mixing the saturated mixture with the unsaturated gas, the aerosol particles continue to evaporate until the mixture is saturated again; thereby decreasing the size of the individual aerosol particles.

The aerosol 16 that leaves the inhaler is merely a carrier and/or transport medium for an active substance, such as a drug. The active substances 30 have to be added to the aerosol. This is schematically indicated in Fig. 6. The active substances 30 are mixed with the aerosol 16. The added substances may combine with the droplets of the aerosol 16, slightly increasing their particle size; however some substances 30 may not combine with the droplets of the aerosol in which case the aerosol 16 functions as a transport medium only.

The original state of the drugs added to the mixer is solid, gas or liquid; however at the point of mixing the active substances 30 are preferably at molecular level.

The aerosol 16 generated in the inhaler 15 will provide the carrier and/or transport medium to deliver active substances from the mixer 35 to the body via the pulmonary route.

In order to further control the aerosol particle size, according to the invention, the aerosol 16 created inside the inhaler 15 will leave the opening 17 with a predetermined temperature which is preferably above body temperature while the dew point of the mixture is below the body temperature. In that case the mixture is still unsaturated and continues to evaporate, even after the aerosol 16 has entered the mouth or nose. On its way to the lungs, the mixture becomes saturated. Since the dew point of the aerosol 16 is set below body temperature, the mixture does not become supersaturated on its way to the lungs. Therefore condensation of the aerosol 16 and thus an increase in aerosol particle size is prevented.

The shown embodiment is a breath-actuated device. That means that the user himself will have to generate the required respiratory effort to create a flow from the fuel cell 1, via the condenser 19, dilution chamber 20, mixer 35 towards the opening 17. The shown embodiment eliminates the need of having a strict breathing co-ordination for administration of the active substances to the lungs.

It should be understood that an alternative solution wherein the airflow is generated without the respiratory effort of a user are also feasible.

With reference to the above it is concluded, that the device and the method as described above provide a cost-effective, clean and sanitary inhalation system. The device provides an accurate, controlled and convenient manner of administering a drug to the body by using an aerosol as carrier. The device provides control over the particle size of the aerosol and is capable of transporting the administered drug (small and large molecules) to the most effective deposition area's in the respiratory tract and the deep lung, without denaturing macromolecules. The device is able to proportionally deliver gases, liquids, or solids.

The device and the method as described above may provide an inhalation drug delivery system for reproducible deep-lung delivery of systemic macromolecular drugs used in the treatment of chronic and subchronic diseases such as diabetes, lung cancer, multiple sclerosis, osteoporosis, and pneumonia. In addition, the device and the method as described above may provide an inhalation system that enhances patient response, compliance and comfort for established indications such as asthma, bronchitis, cystic fibrosis, and emphysema.

Fields as drug and vaccine delivery represent only a small fraction of potential applications that would entail significant process improvements and result in more efficient and consumer-friendly treatment methods. In addition, multiple market segments such as smoking cessation, dietary supplements, aromatherapy, naturopathy - and other Over The Counter (OTC) products may be served with a single portable consumer-end device. Such a device may even be used as a "digital cigarette".

The inhaled drug delivery products market is a billion dollar business expected to grow substantially the coming years. The inhaler according to the invention may be developed in clinical, residential and handheld configurations.

The handheld configuration may be provided with a catalytic burner, in particular a fuel cell which result in a compact and energy self-sufficient personal inhaler. This allows the user to effectively self-administer whatever active substance wherever and whenever with a comfort level that will turn inhalation into recreation.

It must be understood that any other adequate burner and or gas generator can be used without harming the effectiveness of the device and the method.

In analogy to DPI's – Dry-Powder Inhalers – and MDI's – Metered-Dose Inhalers – we refer to our inhalation system as D.E.C.I. or DECI – Deposition Effect Controlled Inhaler.

In the above text wording is used such as 'the human body', 'a patient' etc. It should be understood that the disclosed device and method can be used with the same advantages and effect in the administration of fluids to mammals.



### Claims

1. Device (15) for administration of an aerosol to a mammal, comprising:
  - a chamber (14) provided with gas means, for creating a gas inside the chamber (14),
  - 5 - condensation means, for controlling the pressure and or the temperature inside the device, for creating an aerosol (16) from said gas, and
  - an opening (17) for releasing the aerosol (16) from the device (15),characterised in that,
  - the device (15) is provided with control means for manipulating the condensation  
10 process in order to thereby control the size of the particles of the aerosol (16), prior to releasing the aerosol (16) from the opening (17).
2. Device (15) according to claim 1, wherein the control means are adapted for  
15 decreasing the dew point of the aerosol (16), prior to the release thereof from the opening (17).
3. Device (15) according to claim 1 or 2, wherein the control means comprise dilution  
means for mixing the aerosol (16) with a fluid for decreasing the dew point of the aerosol  
20 (16).
4. Device (15) according to claim 3, wherein the control means comprise supply means  
for mixing the aerosol (16) with an unsaturated gas.
5. Device (15) according to one of the claims 1-4, wherein the device (15) comprises a  
25 gas chamber (14), provided with gas means for creating a gas in the gas chamber (14) and a condensation chamber (19), adjoining the gas chamber (14), provided with condensation means for creating an aerosol (16) inside the condensation chamber (19).
6. Device (15) according to claim 5, wherein the condensation chamber is provided with  
30 temperature means for controlling the temperature of the aerosol (16) inside the condensation chamber (19).

7. Device (15) according to one of the claims 5 or 6, wherein the condensation chamber (19) is provided with pressure means for controlling the pressure of the aerosol (16) inside the condensation chamber (19).

8. Device (15) according to one of the claims 3-7, comprising a dilution chamber (20) for mixing the aerosol (16) with a fluid for decreasing the dew point of the aerosol (16).

9. Device according (15) to claim 5 and 8, wherein the dilution chamber (20) adjoins the condensation chamber (19).

10. Device (15) according to one of the precedings claims, wherein the gas means comprise a fuel cell (1).

11. Device (15) according to one of the preceding claims, wherein the opening (17) for releasing the aerosol (16) is adapted to be connected to the mouth of a mammal, in order to generate a flow through the device (15) by means of the respiratory effort of the mammal.

12. Device (15) according to one of the preceding claims, wherein the device (15) is provided with a mixer (35) for adding an active substance (30) to the aerosol (16), prior to or upon release of the aerosol from the opening (17).

13. Device (15) according to claim 8, wherein the mixer (35) is provided with a line for supplying the active substance (30) to the mixer (35) in the form of a gas or substance-aerosol.

14. Device (15) according to claim 8, wherein the mixer (35) is provided with an opening for supplying the active substance (30) to the mixer (35) in the form of a solid or liquid.

15. Method for administration of an aerosol (16) to a mammal, comprising the steps of:

- creating a gas, by means of gas means, inside a chamber (14),
- condensing at least part of the gas inside the device (15), in order to create an aerosol (16) from said gas,
- releasing the aerosol (16), and
- administration of the aerosol (16) to the mammal,

characterised in that, the method comprises the step of:

- manipulating the condensation process in order to thereby control the size of the particles of the aerosol (16), prior to releasing the aerosol (16) from the opening (17).

5 16. Method according to claims 15, wherein the method comprises the step of:

- decreasing the dew point of the aerosol (16), prior to the administration thereof to the mammal.

10 17. Method according to claim 15 or 16, comprising the step of diluting the aerosol (16) with a fluid for decreasing the dew point of the aerosol (16).

18. Method according to claim 17, comprising the step of diluting the aerosol (16) with an unsaturated gas.

15 19. Method according to one of the claims 15-18, comprising the step of condensing the gas by controlling the temperature in a condensation chamber (19).

20. Method according to one of the claims 15-19, comprising the step of condensing the gas by controlling the pressure in a condensation chamber (19).

20 21. Method according to one of the claims 15-20, comprising the step of generating the gas by means of a fuel cell (1).

25 22. Method according to one of the claims 15-21, comprising the step of making a connection between the mouth of the mammal and the vapour chamber (19) and to generate a flow through the gas chamber (15) for generating a gas, by means of the respiratory effort of the mammal.

30 23. Method according to one of the claims 15-22, comprising the step of adding an active substance (30) to the aerosol (16), prior to or upon release of the aerosol and the administration thereof to the mammal.

24. Method according to claim 23, comprising the step of adding the active substance (30) to the aerosol (16) in the form of a gas or substance-aerosol.

25. Method according to claim 23, comprising the step of adding the active substance (30) to the aerosol (16) in the form of a solid or liquid.



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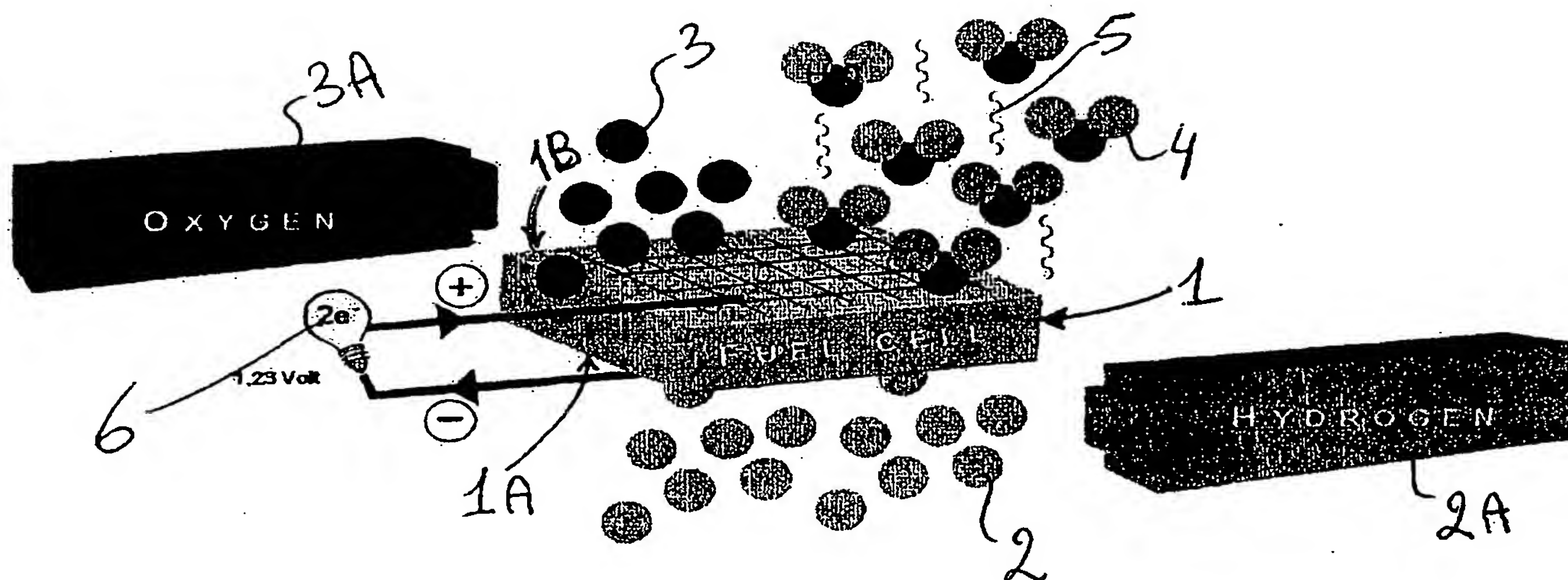


FIG 1

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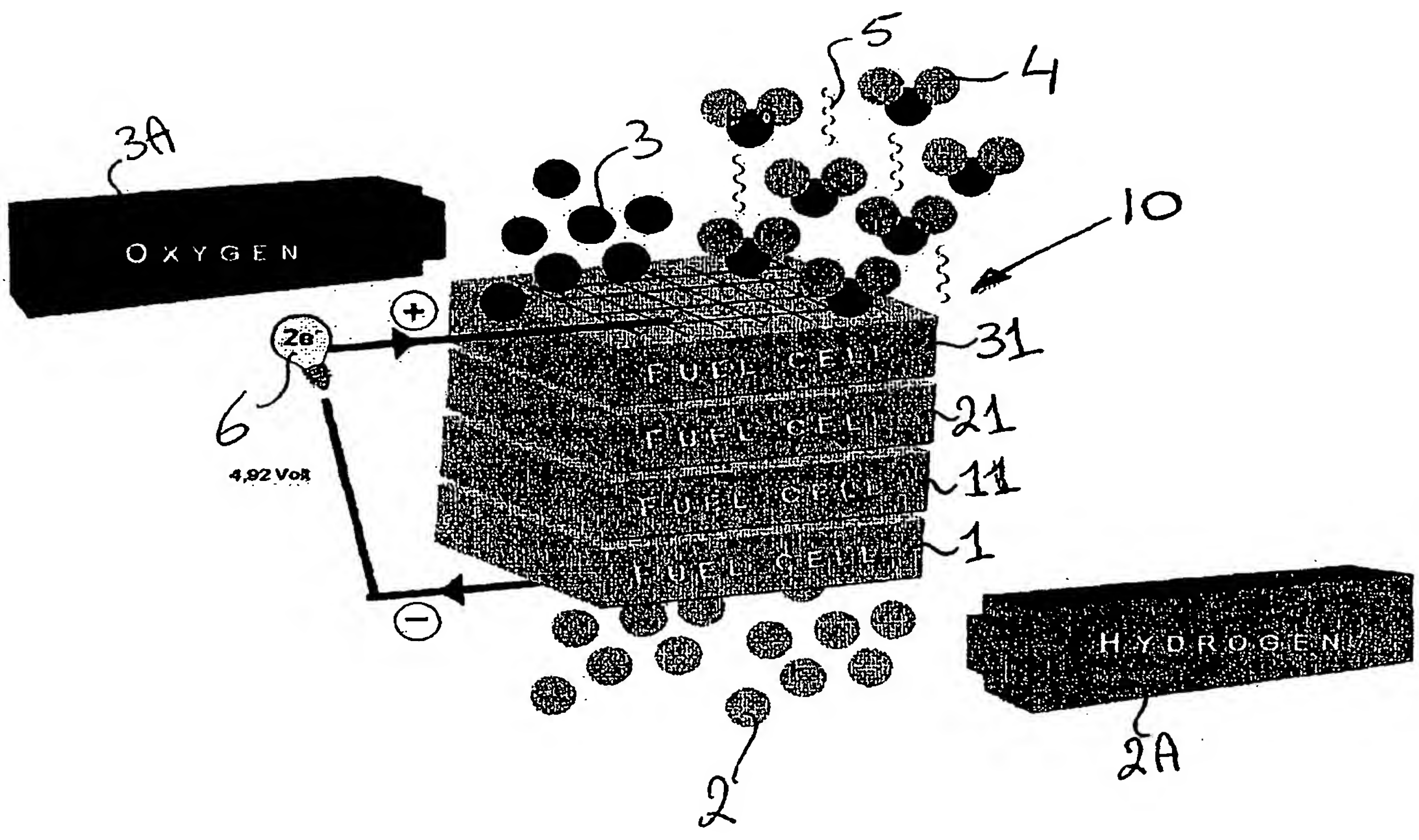


FIG 2

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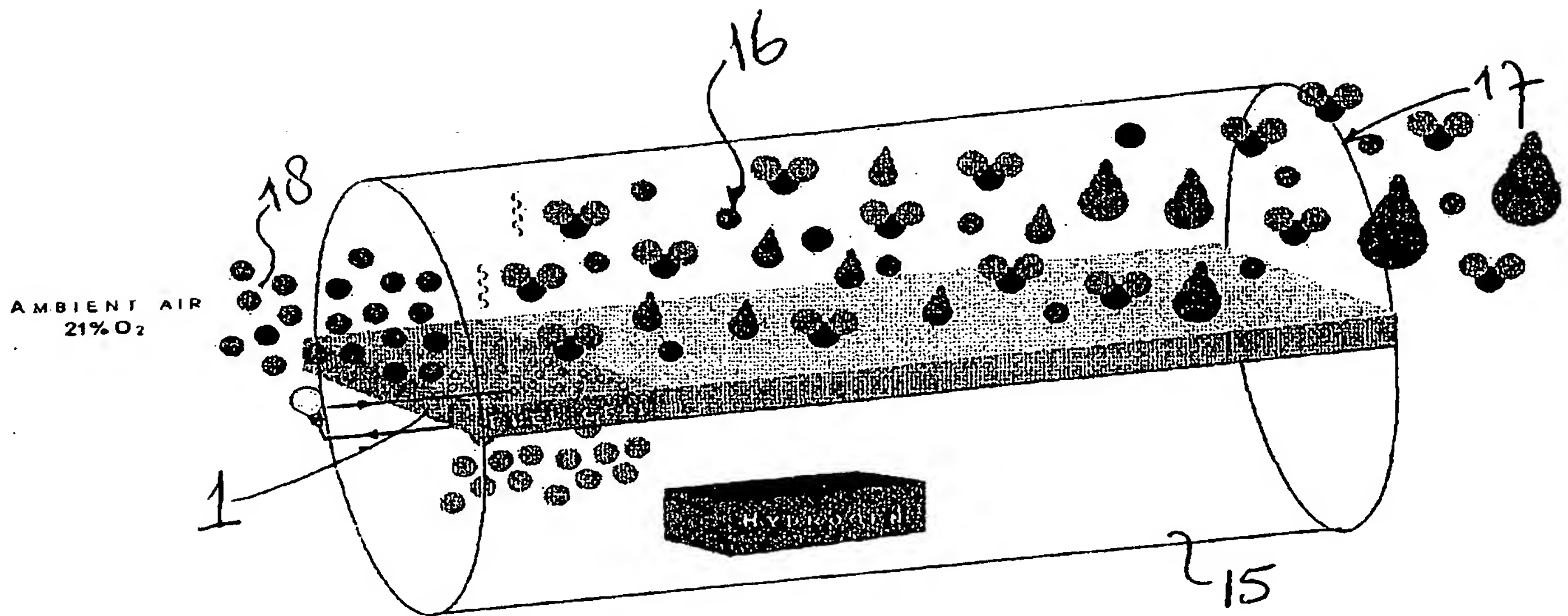


FIG 3

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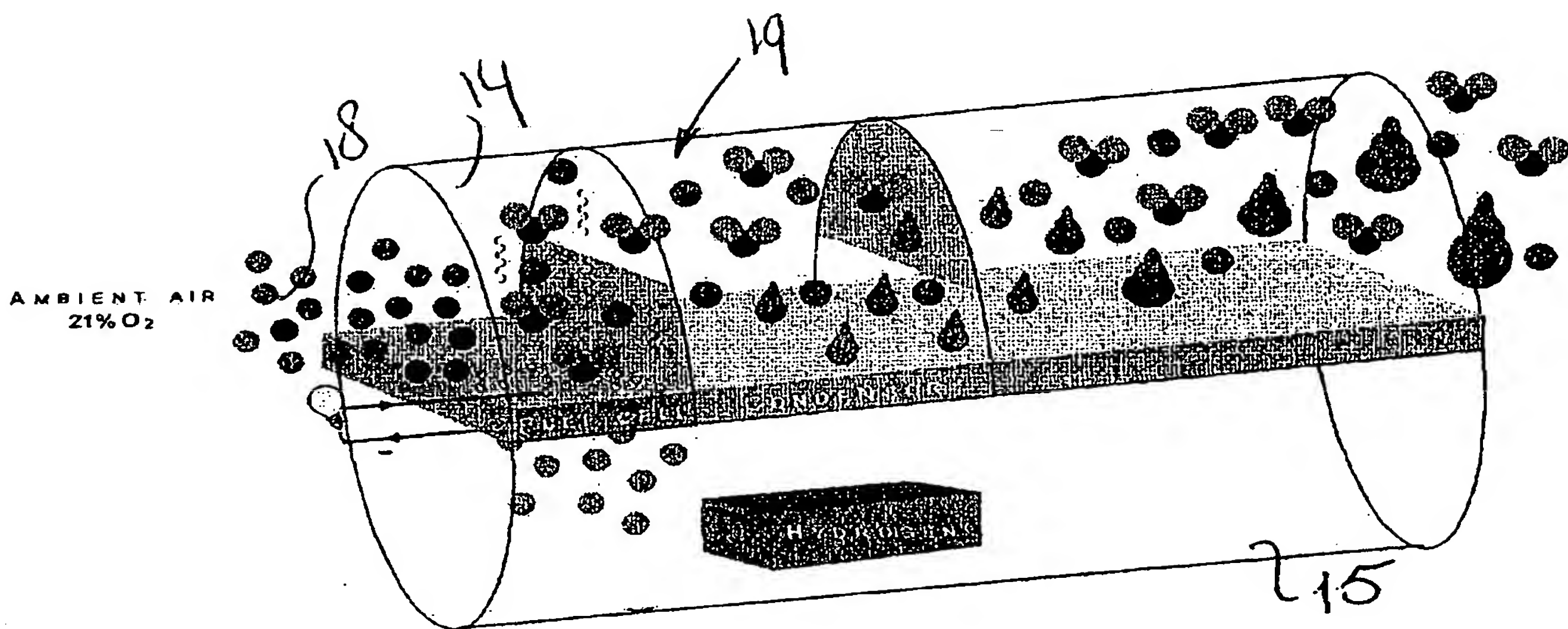
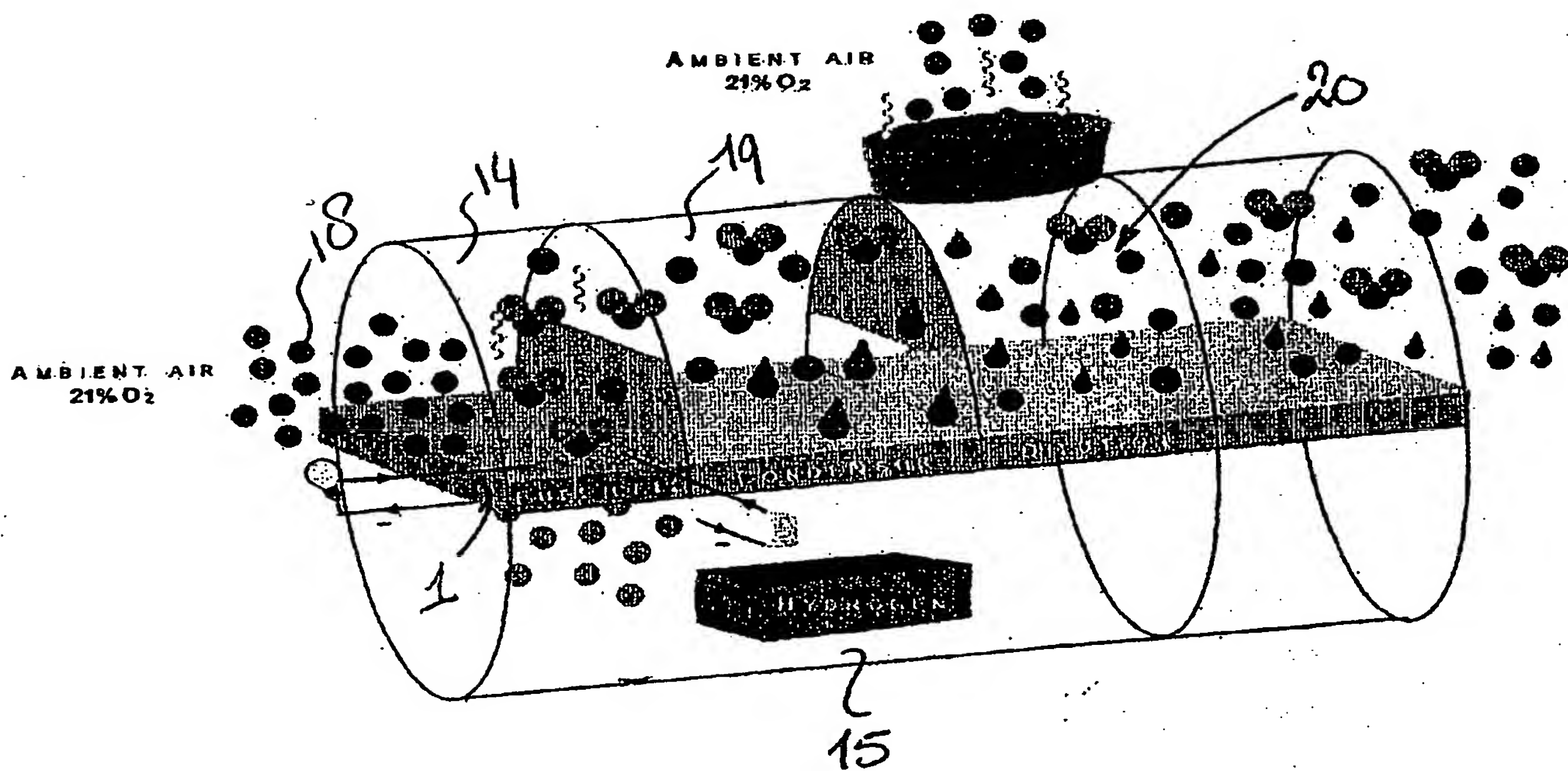


FIG 4



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